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Cutaneous Toxicity Following the Administration of Dactinomycin

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Dactinomycin (AMD) is an effective drug in the management of several malignant disorders and has been used for almost 40 years. Skin and subcutaneous toxicities following extravasation are well known and can be harmful. Similarly radiation-recall is a well established phenomenon following the administration of AMD. We report a patient who developed a localized brawny erythema in the crural folds and the axillae, likely due to AMD. This rare skin complication of AMD seems to benefit from topical corticosteroid treatment, although postinflammatory hyperpigmentation may take months to disappear. Med. Pediatr. Oncol. 29:226–227, 1997. © 1997 Wiley-Liss, Inc.

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INTRODUCTION

Dactinomycin (AMD) is a commonly utilized drug in pediatric oncology. It exerts its antineoplastic effect by intercalating between DNA base pairs in the presence of guanosine, preventing RNA synthesis by blocking DNA transcription [1]. The major toxicity of the drug myelosuppression is well known but a clinically less severe skin side effect is not widely appreciated. In 1995, Kanwar et al., reported two patients with skin rashes following the administration of AMD [2], and provided us with an explanation for a puzzling rash we observed in a patient treated for Wilms tumor.

CASE REPORT

MB, a 13 1/2-year-old Caucasian female, presented with a several week history of anorexia and a one week history of intermittent abdominal pain. Her past history revealed several problems. These included recurrent infections, borderline hypogammaglobulinemia, mild mental retardation, and allergies to penicillin, morphine, codeine, and ipratropium bromide. Physical examination was unremarkable except for a non-tender, firm mass in the right quadrant of the abdomen. No external genitourinary malformations, hemihypertrophy, or aniridia were present. Further work-up revealed a mass in the right kidney, a normal left kidney, and evidence of metastatic disease. A right nephrectomy was performed and histopathologic examination revealed favorable histology Wilms tumor, and a positive lymph node. The patient was thus classified as a stage III Wilms tumor. Consent was obtained from the parents and the patient registered on POG protocol #8650 (NWTS-4) and randomized to receive AMD 45 mg/kg in the first week followed by VCR 1.5 mg/m^2 (maximum dose 2.0 mg) through a central venous line placed at the time of nephrectomy [3]. Radiotherapy of the flank was started three days later. She received a midplane tumor dose of 1080 cGy in six fractions. On the second day of RT, she developed discomfort and irritation in her arm pits. Dermatologic examination revealed brawny erythema in the inguinal regions as well as the axillae in confluent patches with focal areas of follicular accentuation and central desquamation (Figure 1). No bullae were noted. Six days after the administration of AMD, a generalized macular exanthematous eruption developed over the lower abdomen, upper chest, back, and proximal thighs. An erythema with small perifollicular papules also appeared within the radiation port on the right lateral chest. Her medication since admission had included: fentanyl, curare, propofol, succinylcholine, pancuronium, vecuronium, neostigmine, glycopyrrolate, isoflurane, oxygen, and nitrous oxide (all during surgery) bupivacaine and fentanyl in an epidural drip postoperatively, ibuprofen, cephalosporins (cephuroxim iv, cefaclor po), AMD, VCR, ondansetron, dimenhydrinate for breakthrough nausea, docusate sodium (stool softener), and ranitidine (H_2-receptor antagonist) for postoperative heartburn. The generalized macular exanthematous eruption disappeared spontaneously within three days. The brawny erythema in the crural folds and axillae, treated with topical mometasone furoate, slowly regressed, and the affected areas became hyperpigmented (Figure 2). The tanning disappeared over several months.

DISCUSSION

AMD was one of the first drugs demonstrated to have significant antitumor effect in humans, and it has been in

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Fig. 1. Right axilla showing brawny erythema with follicular accentuation and central circular desquamation on day 5 of the reaction.

Fig. 2. The right axilla showing residual hyperpigmentation without desquamation on day 92.

clinical use for almost 40 years. It continues to have a major role in the management of patients with Wilms tumor, Ewing sarcoma, rhabdomyosarcoma, and other soft tissue sarcomas. Patients receiving AMD are at risk of developing several complications. The most common include bone marrow suppression, nausea, vomiting, alopecia, and mucositis [1]. The skin and subcutaneous toxicities of AMD can be particularly noxious when the drug is extravasated [4]. Radiation-recall, wherein a patient receiving AMD develops the erythema characteristic of radiation reaction in skin areas previously exposed to irradiation, is also well-described and can occur as long as 2 years after irradiation [5].

Our patient developed differing dermatologic anomalies after having received many different drugs (as presumably did both the patients reported by Kanwar et al. [2]) as well as radiation therapy in a period of 14 days. It is therefore difficult to determine with certainty which dermatologic lesion was caused by which agent. However, most of the drugs used during this patient's anesthesia are felt to carry a low risk of reactions. The erythema within the radiation port was typical of that caused by the RT and AMD combined. The generalized process is consistent with a drug eruption. The most probable responsible agent was either one of the cephalosporins administered or AMD itself, as has been noted by others [6]. The lesions in the inguinal region and axillae resembled those seen occasionally after busulfan. The Kanwar et al., report prompts us to believe these lesions were most likely caused by AMD, although it is curious that the subsequent administration of the same drug in our patient did not result in recurrence of the rash.

Both the incidence and the mechanism by which AMD causes cutaneous toxicity (immunologic or nonimmune) remain unknown. We therefore believe that such patients should be reported both to alert clinicians and to accumulate experience. We concur with Kanwar et al., that ''Increased awareness of this rare side effect may lead to prompt diagnosis, thereby avoiding unnecessary therapeutic intervention.'' [2].

REFERENCES

1. Riggs CE: Antitumor antibiotics and related compounds. In: MC Perry ed. The chemotherapy source book; Baltimore: Williams & Wilkins, 1992; pp. 318–58.
2. Kanwar VS, Gajjar A, Ribeiro RC, Bowman L, Parham DM, Jenkins III JJ: Unusual cutaneous toxicity following treatment with dactinomycin: A report of two cases. Med Pediatr Oncol 24:329–333, 1995.
3. Green DM, Breslow NE, Evans I, Moksness J, Finklestein JZ, Evans AE, D'Angio GJ: The effect of chemotherapy dose intensity on the hematological toxicity of the treatment for Wilms tumor. Am J Pediatr Hematol Oncol 16:207–212, 1994.
4. Frei E: The clinical use of actinomycin. Cancer Chemother Rep: 58:49–54, 1974.
5. Glaubiger D, Ramu A: Antitumor antibiotics. In: B. Chabner ed. Pharmacologic principles of cancer treatment; Philadelphia: WB Saunders, 1982; pp. 402–7.
6. D'Angio GJ, Bunin NJ: Pediatric toxicity. In John MJ, Flam MS, Legha SS, Phillips TL, eds: Chemoradiation: An integrated approach to cancer treatment, Philadelphia: Lea & Febiger, 1993, p 524.